REMARKS

Claim Listing

Claim	Status		Claim	Status
1 – 17	Cancelled		31	Previously Presented
18	Currently Amended		32	Canceled
19	Cancelled		33	Previously Presented
20	Previously Presented		34 – 35	Cancelled
21	Original		36	Original
22	Cancelled		37 - 50	Cancelled
23	Original		51	Previously Presented
24 – 30	Cancelled		52	New

Prior to this amendment Claims 18-21, 23, 31, 33, 36, and 51 were pending in this application. Claim 19 is cancelled by this amendment, claim 18 is is currently amended, and claim 52 is newly added. Claims are cancelled without prejudice to their assertion in continuation applications.

Claim 18 has been amended to include 2'-O-methyl-5-methyluridine-5'- triphosphate in the list of reactants contacted with the isolated replicase complex. Support for this amendment is found in the application as filed, for example in original Claim 19.

New claim 52 incorporates all of claim 31 as well as 2'-O-methyl-5-methyluridine-5'-triphosphate in the list of reactants contacted with the isolated replicase complex as found in original claim 19.

Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Claim Amendments

Applicants thank the Examiner for an indication that Claim 19 would be allowable except for being dependent on a rejected base claim. Applicants have cancelled Claim 19 and written it intoClaim 18. New claim 52 includes the limitations of claim 52 as well as claim 19. Thus Claims 18 and 52 include 2'-O-methyl-5-methyluridine-5'- triphosphate in the list of reactants contacted with the isolated replicase complex. Support for these amendments is found in the

specification as filed, for example in Claim 19.

Drawings

Applicants submit herewith an amended Figure 1 as requested by the Examiner. Figure 1 has been amended to remove shading from three text boxes that obscured the text within.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 18, 23, 31, 36 and 51 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Hardy et al (Journal of Virology 77(3): 2029-2037, February 2003, cited on the IDS of 09/20/2006) in view of Mueller et al (Journal of Biological Chemistry 261(25): 11756-11764, September 1986).

Claims 20 and 33 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Hardy et al (Journal of Virology 77(3): 2029-2037, February 2003, cited on the IDS of 09/20/2006) in view of Mueller et al (Journal of Biological Chemistry 261(25): 11756-11764, September 1986) as applied to claims 18, 23, 31, 36 and 51 above and further in view of De Francesco et al (US 2002/0164722, prior art of record) and Hess et al (Methods in Enzymology 200: 188-204, 1991, prior art of record.

Claim 21 stands rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Hardy et al (Journal of Virology 77(3): 2029-2037, February 2003, cited on the IDS of 09/20/2006) in view of Mueller et al (Journal of Biological Chemistry 261(25): 11756-11764, September 1986), De Francesco et al (US 2002/0164722, prior art of record) and Hess et al (Methods in Enzymology 200: 188-204, 1991, prior art of record) as applied to claims 20 and 33 above and further in view of Bartenschlager (DE19915178 A1, published October 5, 2000, prior art of record). As the Bartenschlager disclosure is printed in German, US Patent 6,630,343 will be relied upon as a translation. Applicants respectfully traverse these rejections.

Claim 18 and independent claim 52 recite 2'-O-methyl-5-methyluridine-5'- triphosphate in the list of reactants contacted with the isolated replicase complex. None of the applied references teaches or suggests use of 2'-O-methyl-5-methyluridine-5'- triphosphate in a method for quantitating newly initiated RNA or in a method for determining whether a compound is an RNA synthesis initiation inhibitor. Applicants respectfully request the Examiner reconsider and

withdraw the rejections under 35 USC 103(a).

Regarding independent claim 31, the Examiner suggests that Hardy teaches a "method for determining whether a test compound is an RNA synthesis initiation inhibitor of a positive strand RNA virus." This is incorrect. As the Examiner has acknowledged on page 7 of the Office Action, Hardy does not teach hybridizing a probe complementary to the initiation region of the newly synthesized RNA. Hardy is directed to synthesis of replicase RNA by isolated HCV replicons. As explained in the Discussion, Hardy shows that de novo initiation of transcripts may be occurring, but also that elongation is occurring. Hardy does not teach or suggest targeting the initiation region to search for initiation inhibitors, or even that such inhibitors might exist. Hardy teaches, for example, on page 2033, inhibition of RNA synthesis in vitro using inhibitors of compounds directed against the viral polymerase and helicase. Such inhibitors are not RNA synthesis initiation inhibitors as presently claimed. Hardy does not provide the motivation to target the initiation region of the newly synthesized RNAs to test for viral RNA initiation inhibitors.

Mueller is relied upon for the teaching of RNAse protection assays. Mueller teaches hybridizing probes to a variety of regions along the RNA including the site of transcription initiation. (Figure 2) First, Mueller is in the field of transcriptional regulation in yeast mitochondria, specifically relative rates of transcription of yeast mitochondrial genes, and is not concerned with the inhibition of viral RNA synthesis. One of skill in the art of viral inhibition, the subject matter of the present application, would not look to Mueller as it is in a completely different field. Second, even if one were to look to Mueller, there is nothing in either Hardy or Mueller that would direct one to specifically select the transcription initiation region and to look for inhibitors of viral RNA synthesis initiation. Mueller teaches probes to regions throughout the yeast mitochondrial RNA. Hardy teaches an in vitro replication system wherein viral RNAs may be initiated de novo, but are also elongated. Mueller and Hardy provide no specific motivation to select the transcription initiation region from all of the possible sites on the viral transcript. Because Hardy and Mueller do not provide motivation to specifically hybridize a probe to the transcription initiation region of the newly synthesized viral RNA, they do not render obvious a method of selecting inhibitors of viral RNA synthesis. These references do not in any way suggest that such inhibitors are even possible.

As explained in Paragraphs [0092-0093] of the Specification, the claimed assay can distinguish between RNA initiation inhibitors and RNA elongation inhibitors. After RNAse digestion in the claimed assay, the replicon RNA will contain two fractions of replicon RNA: an unlabeled fraction of previously initiated RNAs and a labeled fraction of newly initiated viral replicon RNAs. By detecting the labeled fraction of newly initiated transcripts, newly initiated RNAs can be distinguished from RNAs that were simply elongated from previously synthesized transcripts. In this manner, RNA initiation inhibitors can be distinguished from RNA elongation inhibitors. The combination of Hardy of Mueller does not render obvious a method of identifying RNA initiation inhibitors as presently claimed. The only HCV inhibitors disclosed in these references are disclosed in Hardy and are viral polymerase or helicase inhibitors.

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance are requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

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